

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1. (Canceled)

1 2. (Currently amended) A method for suppressing thymic T cell ~~function~~ maturation of an animal, comprising administering to the animal an amount of a ~~hedgehog~~ agonist polypeptide that includes an N-terminal auto-proteolytic fragment of a hedgehog polypeptide, effective to suppress thymic T cell ~~function~~ maturation, wherein the ~~hedgehog~~ agonist is a polypeptide which includes an ~~hedgehog~~ amino acid sequence selected from that is at least 90% identical to at least one of SEQ ID Nos. 10-18, or any fragment thereof that and binds to a patched polypeptide.

3. (Withdrawn) A method for enhancing the immune system of an animal comprising administering to the animal an immunostimulatory amount of a hedgehog antagonist.

4. (Canceled)

5. (Canceled)

2 6. (Currently amended) The method of claim 1 or 15, wherein the hedgehog amino acid sequence is identical to at least one of SEQ ID Nos. 10-18 ~~or any fragment thereof that binds to a patched polypeptide.~~

3 7. (Currently amended) The method of claim 1 or 15, wherein the ~~hedgehog~~ amino acid ~~sequence~~ polypeptide is encodable by a nucleic acid which hybridizes under stringent conditions of 6.0 x sodium chloride/sodium citrate (SSC) at about 45 °C, followed by a wash of 2.0 x SSC at 50 °C, to at least one of SEQ ID Nos. 1-9.

4 8. (Currently amended) The method of claim 1 or 15, wherein the ~~hedgehog~~ amino acid ~~sequence~~ hedgehog polypeptide is a vertebrate hedgehog polypeptide.

4  
9. (Currently amended) The method of claim ~~2 or 31~~ <sup>4</sup> ~~8~~, wherein the polypeptide includes at least a 50 amino acid ~~extracellular portion~~ N-terminal fragment of a vertebrate *hedgehog* polypeptide.

5 10. (Currently amended) The method of claim ~~2 or 31~~ <sup>4</sup> ~~8~~, wherein the polypeptide includes at least an ~~extracellular portion~~ N-terminal fragment of a vertebrate *hedgehog* polypeptide corresponding to residues 24-194 of SEQ ID No:15.

6 11. (Previously presented) The method of claim ~~7 or 31~~ <sup>1 15</sup> ~~8~~, wherein the polypeptide is modified with one or more lipophilic moieties.

7 12. (Previously presented) The method of claim ~~11~~ <sup>6</sup>, wherein the polypeptide is modified with one or more sterol moieties.

8 13. (Previously presented) The method of claim ~~12~~ <sup>7</sup>, wherein the sterol moiety is cholesterol.

9 14. (Previously presented) The method of claim ~~11~~ <sup>6</sup>, wherein the polypeptide is modified with one or more fatty acid moieties.

10 15. (Previously presented) The method of claim ~~14~~ <sup>9</sup>, wherein each fatty acid moiety is independently selected from myristoyl, palmitoyl, stearoyl, and arachidoyl.

11 16. (Previously presented) The method of claim ~~11~~ <sup>6</sup>, wherein the polypeptide is modified with one or more aromatic hydrocarbons.

12 17. (Previously presented) The method of claim ~~16~~ <sup>11</sup>, wherein each aromatic hydrocarbon is independently selected from benzene, perylene, phenanthrene, anthracene, naphthalene, pyrene, chrysene, and naphthacene.

13 18. (Previously presented) The method of claim ~~11~~ <sup>6</sup>, wherein the polypeptide is modified one or more times with a C7 - C30 alkyl or cycloalkyl.

19. (Withdrawn) The method of claim ~~1~~ <sup>EA</sup>, wherein the *ptc* therapeutic is a small organic molecule.

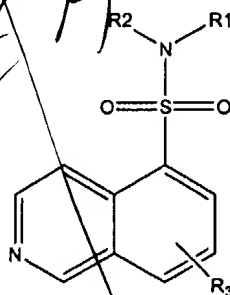
20. (Withdrawn) The method of claim 19, wherein the binding of the *ptc* therapeutic to *patched* results in up- or down-regulation of *patched* and/or *gli* expression.

14 21. (Currently amended) The method of claim 1 or 15, wherein the ~~hedgehog-agonist~~ polypeptide binds to *patched* and mimics *hedgehog* signal transduction by altering the localization, protein-protein binding, and/or enzymatic activity of an intracellular protein involved in *hedgehog* signaling.

22. (Withdrawn) The method of claim 19, wherein the *ptc* therapeutic is an inhibitor of protein kinase A.

23. (Withdrawn) The method of claim 22, wherein the PKA inhibitor is a 5-isoquinolinesulfonamide

24. (Withdrawn) The method of claim 22, wherein the PKA inhibitor is represented in the general formula:



wherein,

R<sub>1</sub> and R<sub>2</sub> each can independently represent hydrogen, and as valence and stability permit a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH<sub>2</sub>)<sub>m</sub>-R<sub>8</sub>, -(CH<sub>2</sub>)<sub>m</sub>-OH, -(CH<sub>2</sub>)<sub>m</sub>-O-lower alkyl, -(CH<sub>2</sub>)<sub>m</sub>-O-lower alkenyl, -(CH<sub>2</sub>)<sub>n</sub>-O-(CH<sub>2</sub>)<sub>m</sub>-R<sub>8</sub>, -(CH<sub>2</sub>)<sub>m</sub>-SH, -(CH<sub>2</sub>)<sub>m</sub>-S-lower alkyl, -(CH<sub>2</sub>)<sub>m</sub>-S-lower alkenyl, -(CH<sub>2</sub>)<sub>n</sub>-S-(CH<sub>2</sub>)<sub>m</sub>-R<sub>8</sub>, or

R<sub>1</sub> and R<sub>2</sub> taken together with N form a heterocycle (substituted or unsubstituted);

R3 is absent or represents one or more substitutions to the isoquinoline ring such as a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido,  $-(CH_2)_m-R8$ ,  $-(CH_2)_m-OH$ ,  $-(CH_2)_m-O$ -lower alkyl,  $-(CH_2)_m-O$ -lower alkenyl,  $-(CH_2)_n-O-(CH_2)_m-R8$ ,  $-(CH_2)_m-SH$ ,  $-(CH_2)_m-S$ -lower alkyl,  $-(CH_2)_m-S$ -lower alkenyl,  $-(CH_2)_n-S-(CH_2)_m-R8$ ;

R8 represents a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle; and

n and m are independently for each occurrence zero or an integer in the range of 1 to 6.

25. (Withdrawn) The method of claim 22, wherein the PKA inhibitor is cyclic AMP analog.
26. (Withdrawn) The method of claim 22, wherein the PKA inhibitor is selected from the group consisting of N-[2-((p-bromocinnamyl)amino)ethyl]-5-isoquinolinesulfonamide, 1-(5-isoquinoline-sulfonyl)-2-methylpiperazine, KT5720, 8-bromo-cAMP, dibutyryl-cAMP and PKA Heat Stable Inhibitor isoform  $\alpha$ .
27. (Withdrawn) A therapeutic preparation of a small molecule antagonist of *patched*, which *patched* antagonist is provided in a pharmaceutically acceptable carrier and in an amount sufficient to modulate the immune system of an adult human patient.
28. (Withdrawn) A method for modulating T lymphocytes maturation, comprising administering to a patient a gene activation construct which recombines with a genomic *hedgehog* gene of the patient to provide a heterologous transcriptional regulatory sequence operatively linked to a coding sequence of the *hedgehog* gene.
29. (Canceled)
30. (Withdrawn) A method of claim 3, wherein enhancing the immune function of an animal comprises stimulating T lymphocyte maturation.

15/31

(Currently amended) A method for suppressing T cell maturation in the thymus, comprising contacting the T cell with an amount of a ~~hedgehog-agonist polypeptide that~~ includes an N-terminal auto-proteolytic fragment of a hedgehog polypeptide, effective to suppress T cell maturation in the thymus, wherein the ~~hedgehog-agonist is a~~ polypeptide ~~which includes an~~ hedgehog-amino acid sequence selected from ~~that is at least 90%~~ identical to at least one of SEQ ID Nos. 10-18, or any fragment thereof that and binds to a *patched* polypeptide.

32. (Canceled)

33. (Canceled)

34. (Canceled)

35. (Canceled)